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이상운동질환
Movement Disorders

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1. 이상운동질환이란?

우리 몸의 움직임은 1) 자동운동(automatic movement), 2) 수의운동 (voluntary movement), 3) 반수의 운동(semi-voluntary movement), 4) 불수의운동(involuntary movement) 등으로 구분할 수 있다. 이상운동질환은 이들 중 반수의운동과 불수의운동을 나타내는 질환을 말한다.

2. 이상운동질환의 분류

이상운동질환은 운동기능감소증(hypokinesia)과 운동과다증(hyperkinesia)로 구분할 수 있다.

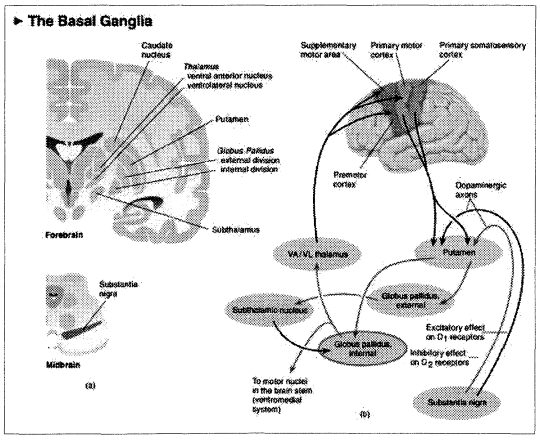

그림 1. 기저핵

1) Hypokinesia
   (1) Akinetic-rigid syndrome
   (2) Apraxia
   (3) Blocking (holiding tic)
   (4) Cataplexy and drop attack
   (5) Catatonia, pshchomotor depression
   (6) Freezing phenomenon
   (7) Hesitant gait
   (8) Hypothyroid slownwss
   (9) Rigidity
   (10) Stiff-muscles

2) Hyperkinesia
   (1) Abdominal dyskinesia
   (2) Akathistic movement
   (3) Asynergy/ataxia
   (4) Athetosis
   (5) Ballism
   (6) Chorea
   (7) Dysmetria
   (8) Dystonia
   (9) Hemifacial spasm
   (10) Hyperkplexia

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(11) Hypogenic syskinesia
(12) Jumpy stumps
(13) Moving toes/fingers
(14) Myoclonus
(15) Myokimia
(16) Myorhythmia
(17) Paroxysmal dyskinesia
(18) Restless legs
(19) Stereotypy
(20) Tics
(21) Tremor

3. 파킨슨병(Parkinson's Disease, PD):

Parkinson's disease is a chronic, progressive neurodegenerative movement disorder. PD results from the degeneration of dopamine-producing nerve cells in the brain, specifically in the substantia nigra. A group of movement disorders that have similar features and symptoms are referred to parkinsonism. PD patients have lost 80% or more of their dopamine-producing cells by the time symptoms appear.

1) The most common form of parkinsonism

2) A slowly progressing, degenerative disease that is usually associated with the following symptoms, all of which result from the loss of dopamine-producing brain cells:
   (1) tremor or trembling of the arms, jaw, legs, and face
   (2) stiffness or rigidity of the limbs and trunk
   (3) bradykinesia -- slowness of movement
   (4) postural instability, or impaired balance and coordination

3) Parkinson's Syndrome, Atypical Parkinson's, or Parkinsonism: PD: primary parkinsonism or idiopathic Parkinson's syndrome

4) Parkinsonism, may include:
   (1) tumors in the brain
   (2) repeated head trauma
   (3) drug-induced parkinsonism - prolonged use of tranquilizing drugs, such as the phenothiazines, butyrophenones, reserpine, and the commonly used drug, metaclopramide for stomach upset
   (4) toxin-induced parkinsonism - manganese and carbon monoxide poisoning
   (5) postencephalitic parkinsonism - a viral disease that causes "sleeping sickness"
   (6) striatonigral degeneration - the substantia nigra of the brain is only mildly affected, while other areas of the brain show more severe damage
   (7) parkinsonism that accompanies other neurological conditions - such as Shy-Drager syndrome (multiple system atrophy), progressive supranuclear palsy, Wilson's disease, Huntington's disease, Hallervorden-Spatz syndrome, Alzheimer's disease, Creutzfeldt-Jakob disease, olivopontocerebellar atrophy, and post-traumatic encephalopathy

5) Four primary symptoms of Parkinson's
   (1) rigidity stiffness when the arm, leg, or neck is moved back and forth
   (2) resting tremor tremor(involuntary movement from contracting muscles) that is most prominent at rest
   (3) bradykinesia slowness in initiating movement
   (4) loss of postural reflexes poor posture and balance that may cause falls; gait or balance problems: small shuffling steps (festination)

6) Other symptoms of Parkinson's disease (PD):
   (1) fatigue or general malaise

(2) trembling
(3) difficulty arising from a seated position
(4) lowered voice volume (dysarthia): soft, whispery voice (hypophonia)
(5) small, cramped, spidery handwriting (micrographia)
(6) losing track of a word or thought
(7) irritability or sadness for no apparent reason
(8) lack of expression in the face
(9) lack of animation
(10) remaining in a certain position for long period of time
(11) unable to normally move arm or leg

7) Secondary or non-motor symptoms of Parkinson's?
(1) depression
(2) senility
(3) difficulty with speaking
(4) emotional changes: anxiety, depression, isolation, fearful and insecure
(5) memory loss and slow thinking
(6) difficulty in swallowing (dysphagia) and chewing: excessive salivation (hypersalivation)
(7) urinary problems or constipation
(8) excessive sweating (hyperhidrosis)
(9) skin problems: scaling, dry skin on the face and scalp (seborrhea)
(10) slow response to questions (bradyphrenia)
(11) sleep problems

8) Risk Factors

In a small number of cases worldwide there is a strong inheritance pattern. A genetic predisposition for PD is possible, with the onset of disease and its gradual development dependant on a trigger, such as trauma, other illness, or exposure to an environmental toxin. The risk increases with age, as PD generally manifests in the middle or late years of life.

9) Causes

Unknown

Free radicals, accelerated aging, environmental toxins, and genetic predisposition.

10) Differential Diagnosis
(1) Medications: antipsychotics (e.g., Haldol and anti-emetics (e.g., Compazine)
(2) Multiple strokes
(3) Hydrocephalus
(4) Progressive supranuclear palsy? degeneration of midbrain structures
(5) Shy-Drager syndrome:atrophy of central and sympathetic nervous systems
(6) Wilson?s disease:copper excretion causes degeneration of the liver and basal ganglia

11) Medical treatment

Levodopa and carbidopa combined (Sinemet) is the mainstay of PD therapy. Levodopa is rapidly converted into dopamine by the enzyme dopa decarboxylase (DDC), which is present in the central and peripheral nervous systems. Much of levodopa is metabolized before it reaches the brain.

Carbidopa inhibits DDC. Combining levodopa with carbidopa increases the amount of levodopa that reaches the brain. Levodopa is most effective in treating bradykinesia and rigidity, less effective in reducing tremor, and often ineffective in relieving problems with balance.

Side effects
(1) Gastrointestinal distress: especially early in treatment, Slow dosage adjustment and taking medication with food can reduce these effects.
(2) Hypotension may occur.
(3) Abnormal movements (dyskinesias) and motor symptom fluctuations are common. Using the lowest effective dose may

prevent or delay the appearance of motor dysfunction.

(4) Depression, confusion, and visual hallucinations may occur, especially in the elderly.

Dopamine Agonists :

(1) Bromocriptine (Parlodel)

(2) Pergolide (Permax)

(3) Pramipexole (Mirapex)

(4) Ropinirole (Requip)

Side effects are similar to those produced by levodopa.

Amantadine (Symmetryl): an antiviral drug with dopamine agonist properties Side effects include mottling of the skin, edema, confusion, blurred vision, insomnia, and anxiety.

MAO-B Inhibitors: Selegiline inhibits MAO-B, increasing the amount of available dopamine in the brain.

Side effects may include nausea, dizziness, abdominal pain, confusion, hallucinations, and dry mouth. Selegiline is contraindicated for patients taking tricyclic antidepressants (e.g., Pamelor), SSRIs (e.g., Prozac), or meperidine (Demerol) and other opiates.

Anticholinergics Anticholinergics reduce the relative overactivity of the neurotransmitter acetylcholine to balance the diminished dopamine activity. This class of drugs is most effective in the control of tremor, and they are used as adjuncts to levodopa.

(1) Benztropine mesylate (Cogentine)

(2) Biperiden (Akineton)

(3) Diphenhydramine (Benadryl)

(4) Trihyxyphenidyl (Artane)

Side effects associated with anticholinergic drugs include dry mouth, blurred vision, constipation, and urinary retention.

COMT(catechol-O-methyl transferase) Inhibitors: augment levodopa therapy by inhibiting the COMT enzyme, which metabolizes levodopa before it reaches the brain; only effective when used with levodopa.

(1) Entacapone (Comtan)

(2) Tolcapone (Tasmar)

Side effects include vivid dreams, visual hallucinations, nausea, sleep disturbances, daytime drowsiness, headache, and dyskinesias.

Other side effects include the following:

(1) Abdominal pain

(2) Constipation

(3) Diarrhea

(4) Discolored urine

(5) Dizziness

(6) Fatigue

(7) Hallucinations

(8) Hyperkinesias

12) Surgical management

- when medication ceases to be effective or when medication side effects, such as jerking and dyskinesias, become intolerable.
- three surgical procedures for treating PD: ablative surgery, stimulation surgery or deep brain stimulation (DBS), and transplantation or restorative surgery.

Ablative Surgery

pallidotomy: is performed to *eliminate uncontrolled dyskinesias.*

Thalamotomy: is performed to *eliminate tremors.*

Deep Brain Stimulation (DBS)

DBS targets the subthalamic nucleus, the targeted region is inactivated, not destroyed, by an implanted electrode (the battery must be replaced every 5 years).

Transplantation or Restorative Surgery: fetal cells, pig embryo cells, stem cells

4. 진전증(Tremor)

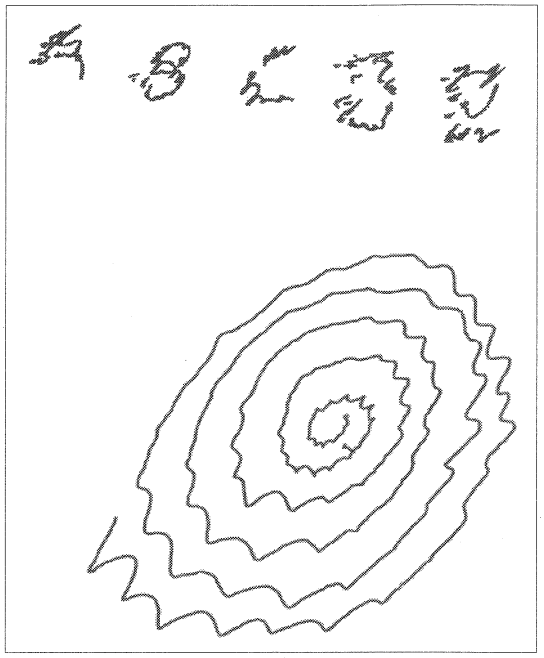

그림 2. 진전증 환자의 쓰기 및 그리기

involuntary trembling in part of the body; most often seen in the hands and head and also may affect the arms, voice (larynx), trunk, and legs.

발병위험 인자 및 원인

(1) Age is a risk factor for essential tremor. It is more common in people over the age of 60.
(2) Family history of the disorder and approximately 50% of cases have a genetic link.o gene ETM1 and gene ETM2.
(3) The cause of essential tremor in people without the genetic mutation is unknown.

증상 및 징후

Symptoms may remain mild or increase in severity over time. Stress, fatigue, anxiety, and hot or cold weather can worsen the disorder.

Differential Diagnosis

Heavy metal poisoning (usually caused by exposure to lead or mercury)

(1) Parkinson' disease
(2) Side effect of medication (e.g., asthma drugs, antidepressants)
(3) Thyroid disease

치 료

Medication

Beta-blockers, such as propranolol (Indural), and antiseizure medications (e.g., primidone [Mysoline], gabapentin [Neurontin]).

Beta-blockers: prescribed for younger patients because they may cause memory loss and confusion in older patients. Other side effects of beta-blockers include dizziness, fatigue, shortness of breath, and nausea.

Side effects of antiseizure medications include drowsiness, nausea, difficulty concentrating, and lack of balance and coordination (ataxia).

benzodiazepines (e.g., diazepam [Valium], clonazepam [Klonopin], alprazolam [Xanax]) and carbonic anhydrase inhibitors (e.g., methazolamide, acetazolamide).

Side effects of benzodiazepines include drowsiness, fatigue, ataxia, and blood clots (thrombosis). Carbonic anhydrase inhibitors may cause tingling in the hands and feet, ringing in the ears (tinnitus), fatigue, and malaise.

Botulinum toxin (Botox) injections treat essential tremor by producing local muscle weakness. When used to treat tremor in the hands, it may cause weakness in the fingers.

Surgery : Thalamotomy: Deep brain stimulation

예 후

Essential tremor is rarely debilitating. Severe cases can usually be treated with medication.

예 방

Essential tremor cannot be prevented.

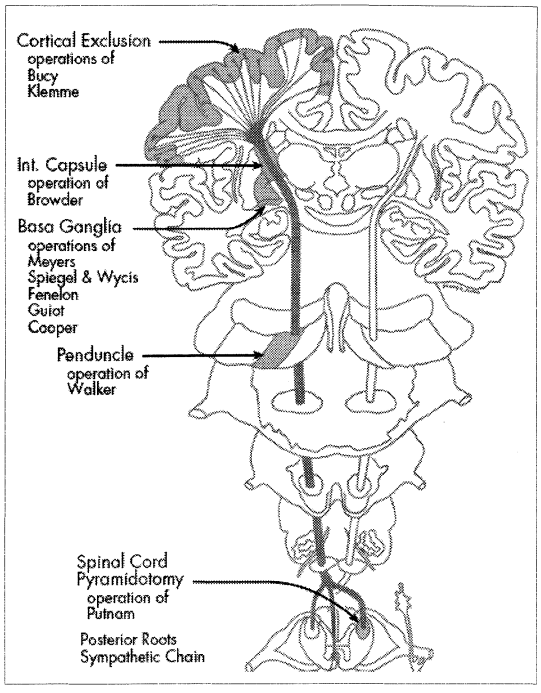

그림 3. 파킨증후군 수술요법의 표적
surgical targets for parkinsonism

5. 헌팅톤병(Huntington's disease, HD)

HD is a fatal hereditary disease that destroys neurons in areas of the brain involved in the emotions, intellect, and movement. The course of HD is characterized by jerking uncontrollable movement of the limbs, trunk, and face (chorea); progressive loss of mental

abilities; and the development of psychiatric problems. AD progresses without remission over 10 to 25 years and patients ultimately are unable to care for themselves. AD usually appears in middle age (30-50 years), but can develop in younger and older people.

Juvenile HD (also called Westphal variant or akinetic-rigid HD) develops before the age of 20, progresses rapidly, and produces muscle rigidity in which the patient moves little, if at all (akinesia).

Causes and Risk Factors

The genetic mutation that occurs in gene IT-15, located on chromosome 4, alters the huntingtin protein, which is present in all human beings, and causes HD.

Signs and Symptoms

HD produces three types of symptoms: movement, cognitive, and psychiatric. The sequence in which symptoms develop varies from person to person.

Movement

Uncontrolled movement, or tics, may develop in the fingers, feet, face, or trunk. This is the beginning stage of **chorea**, involuntary, rapid, ceaseless movement. Chorea can become more intense when the person is anxious or disturbed. Over time other symptoms, such as the following, emerge:

(1) Clumsiness
(2) Jaw clenching (bruxism)
(3) Loss of coordination and balance
(4) Slurred speech
(5) Swallowing and/or eating difficulty
(6) Uncontrolled continual muscular contractions (dystonia)
(7) Walking difficulty, stumbling, falling

Cognitive

Over time judgment, memory, and other cognitive functions begin to deteriorate into dementia. As HD progresses, the ability to concentrate becomes more difficult. The person may have difficulty driving, keeping track of things, making decisions, answering questions, and may lose the ability to recognize familiar objects.

Psychiatric

Early psychiatric symptoms of HD are subtle, varied, and easily overlooked or misinterpreted. Depression is the most common psychiatric symptom of HD and often develops early in the course of the disease. Signs of depression include:

(1) Hostility/irritability
(2) Inability to take pleasure in life (anhedonia)
(3) Lack of energy

Some people develop manic-depression, or bipolar disorder, during the course of the disease.

A person with Huntington?s disease also may exhibit **psychotic behavior**:

(1) Delusions
(2) Hallucinations
(3) Inappropriate behavior (e.g., unprovoked aggression)
(4) Paranoia

In **late-onset disease** (after age 50), the patient may suffer depression rather than experience sudden anger or irritability, and their memory, reasoning, and problem-solving skills may remain sharp.

Early signs of **juvenile HD** often include subtle changes in handwriting and a rapid decline in school performance. The child may develop seemingly minor movement disorders, such as slowness, rigidity, tremor, or rapid muscle twitching. Other early signs of disease may include these changes:

(1) Behavioral changes
(2) Difficulty learning new things
(3) Speech difficulties

Complications

Lack of physical activity, dietary problems, and eating and swallowing problems can cause constipation, incontinence, and weight loss. Psychiatric and cognitive problems can lead to social isolation and deep depression

Diagnosis

Diagnosis is based on a thorough personal and family medical history, physical examination (including a neurological exam), and a series of laboratory tests. The physician will ask about recent changes in intellectual or emotional function, which may be early signs of HD

Genetic Testing

Genetic testing involves taking a blood sample for DNA analysis to determine whether the distinct mutation for HD has occurred in gene IT-15. A sample of DNA also may be required from a closely related affected relative, ideally a parent.

Computed Tomography (CT)

Patients with HD often show shrinkage in two areas of the brain - the caudate nuclei and putamen - and enlargement of cavities within the brain called ventricles. CT scans combined with other procedures such as magnetic resonance imaging (MRI) and/or positron emission tomography (PET) can be a helpful diagnostic tool, especially when evaluated in the context of family history and clinical symptoms.

Treatment

There is no cure for Huntington's disease. Treatment focuses on reducing symptoms, preventing complications, and providing support and assistance to the patient and those close to him or her.

(1) **Medication**
Antipsychotics (hallucinations, delusions, violent outbursts): haloperidol, chlorpromazine, olanzapine (contraindicated if patient has dystonia)
(2) Antidepressants (depression, obsessive-compulsive behavior): fluoxetine, sertraline

hydrochloride, nortriptyline

(3) Tranquilizers (anxiety, chorea): benzodiazepines, paroxetine, venlafaxin, betablockers

(4) Mood-stabilizers (mania, bipolar disorder): lithium, valproate, carbamazepine

(5) Botulinum toxin (dystonia, jaw clenching)

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